CLINICAL TRIALS PLANNING GRANT

Release Date: September 23, 1999

RFA: AR-99-007

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: January 17, 2000

Application Receipt Date: February 17, 2000

THIS RFA USES THE "MODULAR GRANT" AND "JUST-IN-TIME" CONCEPTS. IT INCLUDES DETAILED MODIFICATIONS TO STANDARD APPLICATION INSTRUCTIONS THAT MUST BE USED WHEN PREPARING APPLICATIONS IN RESPONSE TO THIS RFA.

PURPOSE

The purposes of the NIAMS Clinical Trials Planning Grant (CTPG) are: (a) to allow for early peer review of the rationale and design for complex or large-scale clinical trials in those areas that are in the NIAMS mission; and (b) to provide support for the development of a detailed clinical trial research plan, including a manual of operations and procedures, as a means of decreasing the long start-up time often needed for initiating large trials after funding has been awarded.

Investigators who submit applications for complex or large-scale clinical trials for consideration by the NIAMS are expected to provide detailed information regarding the study rationale, design, protocols and procedures, analytical techniques, facilities and environment, administrative procedures, and collaborative arrangements. This information is best presented in a well-documented Manual of Operations and Procedures (MOP) that is submitted as part of the application. However, preparation of a MOP is a time-consuming and expensive activity. The NIAMS Clinical Trials Planning Grant can help support this activity and provide other related assistance.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority

areas. This RFA, Clinical Trials Planning Grant, is related to on or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2000" (Full Report: Stock No. 017-001-00474-0) or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238) or at http://odphp.osophs.dhhs.gov/pubs/hp2000

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Racial/ethnic minority individuals, women, and persons with disabilities are encouraged to apply as Principal Investigators.

MECHANISM OF SUPPORT

The mechanism of support will be the NIAMS Clinical Trials Planning Grant (R21), which will provide up to $75,000 in direct costs for one year. The award cannot be renewed or supplemented. For the purposes of this solicitation the research plan for the application must be limited to 15 pages, and appendix material will not be accepted.

Applicants should be aware that the award of a Planning Grant does not guarantee NIAMS acceptance of the full-scale clinical trial for peer review, nor subsequent funding of the trial following peer review. However, it is expected that the applicant will develop a full-scale clinical trial for submission if the CTPG is approved and funded.

Specific application instructions have been modified to reflect "MODULAR GRANT" and "JUST-IN-TIME" streamlining efforts being examined by the NIH. The modular grant concept establishes specific modules in which direct costs may be requested as well as a maximum level for requested budgets. Only limited budgetary information is required under this approach. The just-in-time concept allows applicants to submit certain information only when there is a possibility for an award. It is anticipated that these changes will reduce the administrative burden for the applicants, reviewers and Institute staff. Complete and detailed instructions and information on Modular Grants can be found at: http://grants.nih.gov/grants/funding/modular/modular.htm

Applications will request direct costs in $25,000 modules, up to a total direct cost request of $75,000. This is a one-year award.

Application budgets will be simplified. Detailed categorical budget information will not be submitted with the application; budget form pages of the PHS 398 application kits will not be used. Instead, total direct costs requested for the one year will be presented. Information, in narrative form, will be provided only for Personnel and, when applicable, for Consortium/Contractual costs. See section on application instructions below.

Other Support pages of the PHS 398 will not be submitted with the application.

Information on research projects ongoing or completed during the last three years of the principal investigator and key personnel will be provided as part of the "Biographical Sketch." This information will include the specific aims, overall goals and responsibilities and should include Federal and non-Federal support. This information will be used by reviewers in the assessment of each individual's qualifications for a specific role in the proposed project.

Following peer review, information about Other Research Support will be requested by NIH from the applicant for applications being considered for award.

Additional budget information will be requested only under special circumstances.

FUNDS AVAILABLE

It is estimated that $500,000 total costs will be available for support of this initiative. Direct costs will be awarded in modules of $25,000, less any overlap or other necessary administrative adjustments. Facilities and Administrative costs will be awarded based on the negotiated rates. Awards are contingent on the availability of funds and the receipt of highly meritorious applications.

RESEARCH OBJECTIVES

The purpose of this Request for Applications is to stimulate early planning for complex or large-scale clinical trials. This solicitation is to provide support for the extensive efforts required to develop a detailed clinical trial research plan which may include detailed information regarding the study rationale, design, protocols and procedures, analytical techniques, facilities and environment, administrative procedures, and to organize an effective group of investigators. After the basic design and rationale for a large-scale or complex clinical trial have been determined, the CTPG will support the development of the specific aspects of the trial which will be essential to the conduct of a full-scale clinical trial. This information is best presented in a well-documented

Manual of Operations and Procedures (MOP) that is submitted as part of the application/proposal for the clinical trial. However, preparation of a MOP is a time-consuming and expensive activity. The NIAMS Clinical Trials Planning Grant can help support this activity and provide other related assistance.

Detailed information regarding the rationale of the clinical trial, based on adequate, preclinical science and preliminary clinical research, must be developed prior to submission and included in the CTPG application. The purpose of the planning grant is not to support studies to obtain preliminary data or to conduct studies to support the rationale for the clinical trial.
The expected product of the planning grant is a detailed clinical trial research plan including a complete manual of operations and procedures.

Any disease area that is within the NIAMS mission is appropriate for consideration under this RFA.

SPECIFIC REQUIREMENTS TO BE ADDRESSED IN THE CTPG APPLICATION

The CTPG applications will be evaluated based on the documentation provided for: (1) the RATIONALE of undertaking a clinical trial (CT) in the proposed research area (not the rationale for submitting the CTPG application); (2) the APPROACH to be used during the one year funding of the CTPG to develop the detailed planning (to be documented in a MOP) for the CT; (3) innovative plans and activities to be used in accomplishing the goals of the CT; (4) the expertise of INVESTIGATORS and other members of the CT investigative team; (5) the ENVIRONMENT for conducting the CT; and (6) the adequacy of plans to address the NIH INCLUSION POLICIES in the CT. The planning grant application will NOT be evaluated for the research plan, design, etc. of the future clinical trial.

The following should be part of a CTPG application:

1. RATIONALE (Background, Significance, Preliminary Studies). The background and significance of the application must address the rationale for a future, full-scale clinical trial (CT) in the proposed area including: a clear statement of the question that a CT would address; reasons for selection of intervention(s) and mode(s) of delivery including specific details such as dose or a particular procedure; the biological mechanisms and clinical data that support conducting a CT; information adequate to determine the significance and need to perform a CT; compelling need to proceed with a CT as soon as possible (e.g. impact on health care); competitive therapies--advantages and disadvantages; ethical issues surrounding a CT.

2. APPROACH (Experimental Design).

The application for a CTPG should NOT include a full description of the experimental design of the future RCT. However, it must show how these items will be addressed during the one-year planning period in order to develop the plan for the RCT: including translation of the clinical question into a statistical hypothesis; sample size and duration of the CT; endpoint(s), outcome measures, and data to be collected; randomization, masking, and inclusion/exclusion criteria; the strengths and weaknesses of the proposed methods, and possible alternatives; ancillary therapies; capability to develop methods for standardization of procedures for data management and quality control; plans to address patient recruitment/retention; plans for documenting the availability of the requisite eligible patient pool; plans for including women and minority individuals as trial participants and plans for recruitment outreach, as appropriate; follow-up procedures to ensure adherence to protocols, retention of subjects, and collection of data at stated intervals.

3. INNOVATION.

Any innovations planned for the full CT should be highlighted. Innovations will be an important consideration in evaluating the CT.

4. INVESTIGATORS.

The application must include a clear statement of the leadership and proposed organization of the CT, including: identification of a principal investigator, and, for multi-center trials, identification of study investigators at each of the sites; professional training and experience of the trial organizers in such areas as the clinical problem under study, administration of complex projects, and study design; inclusion of statisticians, data managers and study coordinators; use of study monitors in multi-site studies; plans to add or drop centers; essential committee structure, i.e., Planning, Steering, Executive, Publication, Data and Safety Monitoring.

5. ENVIRONMENT.

Enough information should be provided to evaluate the potential success of the RCT in terms of patient availability, administrative support, available resources, data analysis support, etc.

6. INCLUSION POLICIES.

The adequacy of conformance with the following NIH Guidelines.

Inclusion of Women and Minorities in Research Involving Human Subjects:

It is the policy of the NIH that women and members of minority groups and their subpopulations must be included in all NIH supported biomedical and behavioral research projects involving

human subjects so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study. If women or minorities are excluded or inadequately represented a clear compelling rationale must be provided. All investigators proposing research involving human subjects should read the "NIH Guidelines For Inclusion of Women and Minorities as Subjects in Clinical Research," which have been published in the Federal Register of March 28, 1994 (FR 59 14508-14513) and reprinted in the NIH Guide for Grants and Contracts, Volume 23, Number 11, March 18, 1994. This information is available on the Internet at: http://ohrp.osophs.dhhs.gov/humansubjects/guidance/59fr14508.htm

Inclusion of Children as Participants in Research Involving Human Subjects:

It is the policy of the NIH that children must be included in all human subjects research conducted or supported by the NIH unless there are scientific or ethical reasons not to include them. The goal of the policy is to increase the participation of children in research to obtain appropriate data. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998. The policy does not apply to ongoing studies (e.g., Type 5, Type 2) or previously reviewed amended applications. All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts, March 6, 1998. This information is available on the internet at http://grants.nih.gov/grants/guide/notice-files/not98-024.html

Investigators also may obtain copies of the policies on "Inclusion of Women and Minorities in Research Involving Human Subjects" and "Inclusion of Children as Participants in Research Involving Human Subjects" from the program staff listed under INQUIRIES. Program staff may also provide additional relevant information concerning the policy.

LETTER OF INTENT

Prospective applicants are asked to submit, by January 17, 2000, a letter of intent that includes a title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

The letter of intent is to be sent to: Tommy L. Broadwater, Ph.D. at the address listed under INQUIRIES.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 4/98) is to be used in applying for these grants, with the modifications noted below. These forms are available at most institutional offices of sponsored research; from the Division of Extramural Outreach and Information Resources, National Institutes of Health, 6701 Rockledge Drive, MSC 7910, Bethesda, MD 20892-7910, telephone 301/435-0714, e mail: grantsinfo@nih.gov; and on the Internet at http://grants.nih.gov/grants/funding/phs398/phs398.html

The RFA label available in the PHS 398 (rev. 5/95) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title (NIAMS Clinical Trials Planning Grant) and number (RFA AR-99-007) must be typed on line 2 of the face page of the application form and the YES box must be marked.

The sample RFA label available at: http://grants.nih.gov/grants/funding/phs398/label-bk.pdf has been modified to allow for this change. Please note this is in pdf format.

BUDGET INSTRUCTIONS

The total direct costs must be requested in accordance with the program guidelines and the modifications made to the standard PHS 398 application instructions described below:

o FACE PAGE: Items 7a and 7b should be completed, indicating Direct Costs (in $25,000 increments up to a maximum of $75,000 and Total Costs [Modular Total Direct plus Facilities and Administrative (F&A) costs] for the one year budget period. Items 8a and 8b should be completed.

o DETAILED BUDGET FOR THE INITIAL BUDGET PERIOD - Do not complete Form Page 4 of the PHS 398. It is not required and will not be accepted with the application.

o BUDGET FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT - Do not complete the categorical budget table on Form Page 5 of the PHS 398. It is not required and will not be accepted with the application.

o NARRATIVE BUDGET JUSTIFICATION - Use a Modular Grant Budget Narrative page.

(See http://grants.nih.gov/grants/funding/modular/modular.htm for sample pages.) At the top of the page, enter the total direct costs requested for each year.

o Under Personnel, list key project personnel, including their names, percent of effort, and roles on the project. No individual salary information should be provided.

For Consortium/Contractual costs, provide an estimate of total costs (direct plus facilities and administrative) for each year, each rounded to the nearest $1,000. List the individuals/organizations with whom consortium or contractual arrangements have been made, the percent effort of key personnel, and the role on the project. Indicate whether the collaborating institution is foreign or domestic. The total cost for a consortium/contractual arrangement is included in the overall requested modular direct cost amount.

Provide an additional narrative budget justification for any variation in the number of modules requested.

o BIOGRAPHICAL SKETCH - The Biographical Sketch provides information used by reviewers in the assessment of each individual's qualifications for a specific role in the proposed project, as well as to evaluate the overall qualifications of the research team. A biographical sketch is required for all key personnel, following the instructions below. No more than three pages may be used for each person. A sample biographical sketch may be viewed at: http://grants.nih.gov/grants/funding/modular/modular.htm.

- Complete the educational block at the top of the form page;
- List position(s) and any honors;
- List selected peer-reviewed publications, with full citations;
- Provide information, including overall goals and responsibilities, on research projects ongoing or completed during the last three years.

o CHECKLIST - This page should be completed and submitted with the application. If the F&A rate agreement has been established, indicate the type of agreement and the date. It is important to identify all exclusions that were used in the calculation of the F&A costs.

o The applicant should provide the name and phone number of the individual to contact concerning fiscal and administrative issues if additional information is necessary following the initial review.

APPLICATIONS NOT CONFORMING TO THESE GUIDELINES WILL BE CONSIDERED UNRESPONSIVE TO THIS RFA AND WILL BE RETURNED WITHOUT FURTHER REVIEW.

Submit a signed, typewritten original of the application and three signed photocopies in one package to:

CENTER FOR SCIENTIFIC REVIEW
NATIONAL INSTITUTES OF HEALTH
6701 ROCKLEDGE DRIVE, ROOM 1040 - MSC-7710
BETHESDA MD 20892-7710
Bethesda MD 20817 (for express/courier service)

At the time of submission, send an additional two copies of the application to Dr. Tommy L.Broadwater at the address listed under INQUIRIES. It is important to send these two copies at the same time as the original and three copies are sent to the Center for Scientific Review (CSR). These copies are used to identify conflicts and help ensure the appropriate and timely review of the application.

Applications must be received by February 17, 2000. If an application is received after that date, it will be returned to the applicant without review. The Center for Scientific Review (CSR) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by CSR and responsiveness by NIAMS staff. Incomplete or unresponsive applications will be returned to the applicant without further consideration.

Applications that are complete and responsive will be evaluated for scientific and technical merit by a Special Emphasis Panel convened by the NIAMS Review Branch. As part of the initial merit review, all applications will receive a written critique but may undergo a streamlined peer review process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed, assigned a priority score, and receive

a second level review by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments reviewers will be asked to discuss the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that the application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

The criteria should be used to evaluate CTPG applications based on the "Specific Requirements To Be Addressed In The Application" as spelled out in an earlier section of these guidelines.

SIGNIFICANCE: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

INNOVATION: Does the project employ novel concepts, approaches or method?
Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

INVESTIGATORS: Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)?

ENVIRONMENT: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the

scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

In addition, reviewers will be asked to assess the adequacy of conformance with the NIH Guidelines for the Inclusion of Women, Minorities and Children as Subjects in Clinical Research, the provisions for the protection of human subjects and the safety of the research environment.

AWARD CRITERIA

Applicants should be aware that, in addition to scientific merit, program priorities and balance, the total costs of the proposed project and the availability of funds will be considered by NIH staff as well as recommendations by the NIAMS Advisory Council in making funding decisions.

Schedule:
Letter of Intent Receipt Date: January 17, 2000
Application Receipt Date: February 17, 2000
Date of Initial Review: June/July 2000
Review by Advisory Council: September 14, 2000
Anticipated Award Date: September 29, 2000

INQUIRIES

Inquiries concerning this RFA are encouraged. Additional information, including sample budget narratives and biographical sketch, may be found at this site: http://grants.nih.gov/grants/funding/modular/modular.htm. The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct letters of intent to:

Tommy L. Broadwater, Ph.D.
Scientific Review Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
45 Center Drive, Room 5AS-25U, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-4952
FAX: (301) 480-4543
Tommy_Broadwater@nih.gov

Direct inquiries regarding programmatic issues to one of the following persons, according to scientific area:

Dr. Richard W. Lymn
Muscle Biology
45 Center Drive, Room 5AS-49E, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-5128
FAX: (301) 480-4543
Email: Richard_W_Lymn@nih.gov

Dr. Joan McGowan
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Dr. Susana A. Serrate-Sztein
Rheumatic Diseases

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Bethesda, MD 20892-6500
Telephone: (301) 594-5032
FAX: (301) 480-4543
Email: Susana_Serrate-Sztein@nih.gov

Direct inquiries regarding fiscal matters to:

Sally A Nichols
Grants Management Office
National Institute of Arthritis and Musculoskeletal and Skin Diseases
45 Center Drive, Room 5AS-49F, MSC 6500
Bethesda, MD 20892-6500
Telephone: (301) 594-3535
FAX: (301) 480-5450
Email: Sally_Nichols@nih.gov

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.846. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410), as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and promote the non-use of all tobacco products. In addition, public law 103-227, the pro-children act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the America people.

Return to Volume Index
Return to NIH Guide Main Index